Evaluation of Children Exposed to Infectious Tuberculosis (TB): Recommendations for Pediatric Primary Care

Background

Children are at increased risk of progression from latent tuberculosis infection (LTBI) to tuberculosis (TB) disease compared to adults and are at higher risk of developing severe TB disease. This risk is especially high for children <5 years old; studies have shown that on average 5% of children screened for TB after an exposure are found to have TB disease at the time of screening. Outcomes of TB disease for young children can be particularly devastating – including death and lifelong disability, especially among those with central nervous system (CNS) disease.

Risk for progression of LTBI to TB disease is especially high for children <5 years old.

Therefore, children identified as having been a close contact to someone with infectious tuberculosis are a priority for testing. ***The goals of evaluation are to identify and treat children with both active or symptomatic TB disease and asymptomatic LTBI.***

TB evaluation overview

The essential components for evaluation of pediatric contacts to TB include:

1. Evaluate for signs/symptoms of TB disease
2. Review vitals and weight and perform a complete physical exam
3. Review results of Interferon Release Assay (IGRA) or Tuberculin Skin Test (TST)
4. Review a chest x-ray (CXR) (posteroanterior [PA] and lateral for kids <5 years old)
5. Treat TB disease and LTBI, as determined by the above results

Evaluate for signs/symptoms of active TB disease

The clinical presentation of TB can be subtle and similar to common pediatric infectious diseases, especially early in the disease process. It is important to remember that TB can manifest in any organ system and young children are more likely to have disseminated TB disease. Common signs or symptoms include fever, poor weight gain or weight loss, cough or respiratory distress, and lymph node enlargement. Signs of meningitis, encephalitis, and hydrocephalus must also be evaluated. Less common, but potentially important clues of TB in children include prolonged or unexplained general irritability, abdominal symptoms such as pain or diarrhea, headache/confusion, dysuria/hematuria, or extremity or back pain. ***Signs or symptoms potentially consistent with TB disease, especially for children with a known TB exposure, warrants further investigation***.

For a child with known TB exposure, signs or symptoms potentially consistent with TB disease warrant further evaluation.

Physical exam

TB can present in any organ system, so a thorough exam is important. In young children poor weight gain is often a marker of TB disease in a TB-exposed child. The exam should include all organ systems with focus evaluation on the child's lungs, abdomen, central nervous system, and lymph nodes. Some TB-suspicious physical exam findings include crackles/decreased air movement, stridor/wheezing, muffled heart sounds, hepato-splenomegaly, abdominal pain to palpation, peripheral lymph node enlargement (especially cervical chain, axillary, or

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inguinal), or findings consistent with central nervous system involvement (confusion, irritability, ataxia, or weakness). More rare findings can include otitis media or persistent skin rashes.

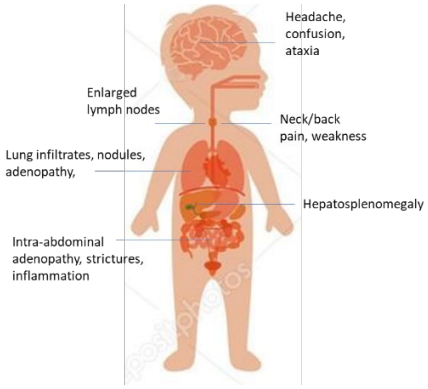


Image Source: Post it Photos

Perform Interferon-Gamma Release Assay (IGRA) or Tuberculin Skin Test (TST)

IGRA and TST help identify people infected with TB bacteria; they do not differentiate between TB disease and LTBI. These tests can be falsely negative within 8-10 weeks of TB exposure as the delayed-type immune response develops; a definitive test should occur ***8-10* weeks** after the last possible TB exposure. Management of children during this interval is described below under "Window Prophylaxis". For children with TB disease, IGRA or TST can be helpful diagnostic tools when positive but can be falsely negative. IGRA/TST are insufficiently sensitive for identifying TB in children younger than 4 months of age; these children should be treated either for TB disease or with Window Prophylaxis until a definitive IGRA/TST is obtained, in consultation with a pediatric TB expert^. Treatment for TB disease should occur in children with signs or symptoms of TB disease regardless of TB test results. ***A negative TB test alone does not rule out TB disease.***

Evaluation for TB is not complete until ≥ 8 weeks after last exposure to TB.

A negative TST or IGRA alone does not rule out TB disease.

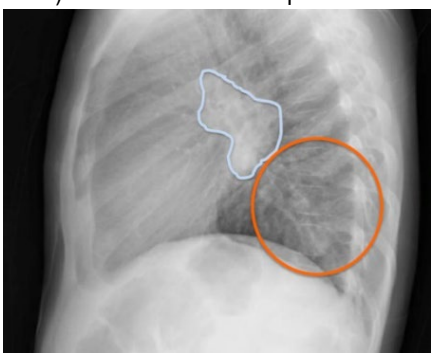
IGRAs such at the QuantiFERON-TB Gold Plus (QFT) or the T-SPOT are the preferred tests for children of all ages based on improved specificity for TB infection particularly among BCG-vaccinated children. IGRAs require a blood draw, but a single patient visit; special attention to the manufacturer's collection and handling instructions is necessary to ensure accurate results. TSTs can be falsely positive among children with previous BCG vaccination, require knowledgeable staff for placement and reading, and require a follow-up patient visit for reading the skin induration. Indeterminate tests should be repeated using IGRA. Best practice is to repeat the same test used for initial testing for any follow-up testing after the 8–10-week window.

Chest x-rays (CXR)

CXR should be performed in children with any of the following:

- Signs or symptoms of TB disease
- Positive IGRA or TST
- Exposure to infectious TB (within the last 8 weeks) regardless of TB test result and:
    - Immunocompromising condition or
    - Age <5 years

Children < 5 years old with recent TB exposure should get both PA and lateral views as intrathoracic adenopathy is a common finding of early TB that can often only be seen on a lateral chest film (example below). Consultation with a pediatric radiologist or child TB expert^ might be indicated.



Source: The Curry International Tuberculosis Center

Management

Suspicion for active TB disease – Children with signs or symptoms of TB disease, clinical exam, or CXR consistent with active TB should undergo collection of sputum, gastric aspirates, urine, and/or stool (along with other body fluids depending on suspected location of disease) for acid fast bacilli (AFB) culture, AFB smear, and TB polymerase chain reaction (PCR) regardless of TB test result; children suspected of having TB should be promptly reported to the local public health department. Empiric treatment should often be initiated for sick children; clinical consultation with pediatric ID, the public health TB program, and/or a TB expert^ should guide work-up and treatment. Children often have pauci-bacillary TB and cultures are frequently negative despite TB disease; treatment is often a clinical decision.

LTBI – Children with appropriate growth, normal physical exam and CXR, and who lack signs and symptoms of TB disease but have a positive IGRA or TST should be treated for LTBI. Treatment options include (preferred options in **bold**):

- **4R: 4 months of daily rifampin** (15-20 mg/kg daily, max 600mg)
- **3HP: 12 doses of isoniazid* and rifapentine** (dosed weekly by weight for children ≥2 years); dosing information here.
- *3HR*: 3 months of daily isoniazid* (10 mg/kg; max dose 300mg) and rifampin (15-20 mg/kg; max dose 600mg)
- *6H or 9H:* 6-9 months of daily isoniazid* (10 mg/kg daily; max dose 300mg)
  **B6 should be taken with isoniazid for exclusively breastfed infants.*

Window prophylaxis – Children with appropriate growth, a normal exam, without signs or symptoms of TB disease, a negative IGRA or TST (or age <4 months), and a normal CXR who were exposed to tuberculosis within the last 8 weeks and are under age 5 years old or immune compromised, window prophylaxis should be provided until a definitive TB test can be obtained *8-10* weeks after last exposure to infectious tuberculosis. Children <5 years of age and immunocompromised children are at high risk of TB progression and the TB tests can be falsely negative soon after exposure. Any LTBI regimen above (4R, 3HP, 3HR, 6H or 9H) can be started as window treatment. Children with a positive IGRA or TST at the end of window (8-10 weeks after last exposure) should finish the full LTBI treatment course. Doses of medicine given during the window period count towards the LTBI treatment course. A negative IGRA or TST at the end of the 8-10-week window means treatment can stop. No repeat CXR is required at the end of the window unless the child has new symptoms.

No treatment - Children older than 4 months of age with appropriate growth, a normal physical exam, and a negative IGRA/TST that was obtained 8-10 weeks after the last possible exposure to tuberculosis and without signs or symptoms of TB disease do not require TB treatment.

^Pediatric TB expertise available through many local public health departments, California Department of Public Health TB control (tbcb@cdph.ca.gov) or the Curry International TB Center Warmline (Currytbcenter@ucsf.edu).

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